Hepatitis C Virus: National Trends and Prevention Recommendations

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Centers for Disease Control and Prevention

Goals

- **Describe:**
- Trends in HCV transmission, disease, and mortality
- Health benefits of HCV testing, care, and treatment
- Strategies to screen and link HCV infected persons to care

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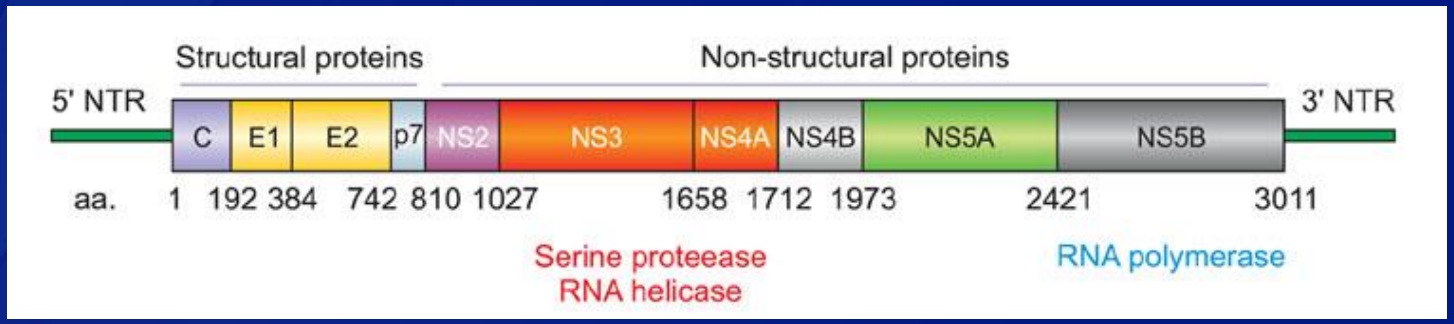
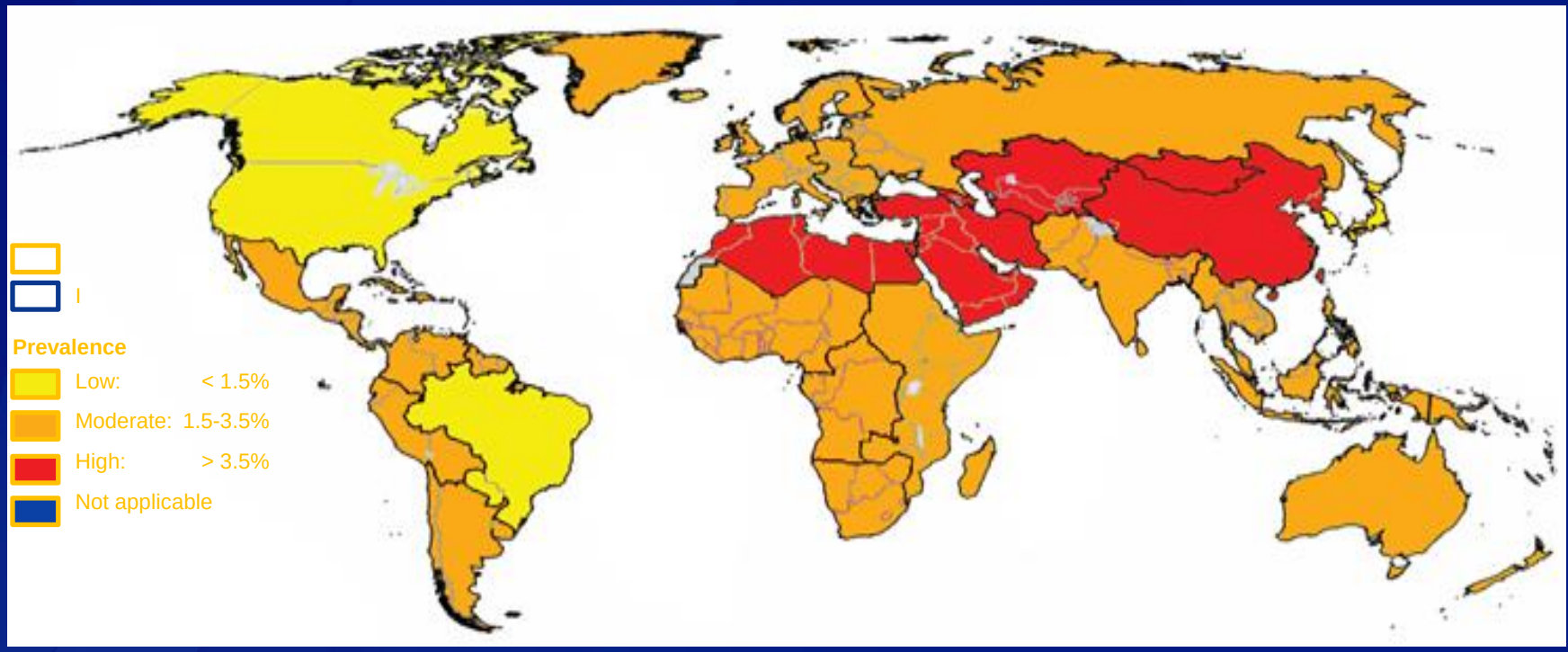
Hepatitis C Virus

- Discovered in 1989, RNA virus, family *Flaviviridae*
- 9600 nucleotide genome- single polyprotein
  - Non-structural protein- targets of therapy
  - High genetic diversity – intra-host variants- "quasispecies"
  - 7 major genotypes- varied response to treatment
    - Genotype 1- ~ 70% of infections in US
  - No vaccine



Lindenbach BD, Fields virology. Philadelphia, 2001. Simmonds P, *Hepatology* 1995. Irshad M, *Hepatogastroenterology*. 2010. Manos MM, *J Med Virol* 2012; Alter HJ, Gastroenterol Hepatol.. 1990; Choo QL, Science 1990

Global Hepatitis C Burden is Large and Highest in Asia and Africa



- 3-4 million new infections per year
- 130-150 million chronic infections
- 704,000 deaths/ 2010

Liver International. WHO unpublished data; pages 1-3, June 8, 2012; Perz JF, et al. *J Hepatol*. 2006; Zhuang X, et al. *Drug Alcohol Depend.* 2012; Serano L, et al. *J Int Assoc Physicians AIDS Care (Chic).* Jul 24, 2012; Pitt L, et al. *Eur J Public Health.* 2009;76P. http://www.who.int/mediacentre/factsheets/fs164/en/

Prevalence of Current HCV Infection Among Persons in the United States

Prevalence Civilian, Non-Institutionalized Populations (NHANES)	2.7 million (2.2-3.2 million) 1.0% (0.8%-1.2%)
Estimated HCV Infection Among Homeless and Incarcerated Persons (Not Included in NHANES)	360,000-840,000 22%-52%

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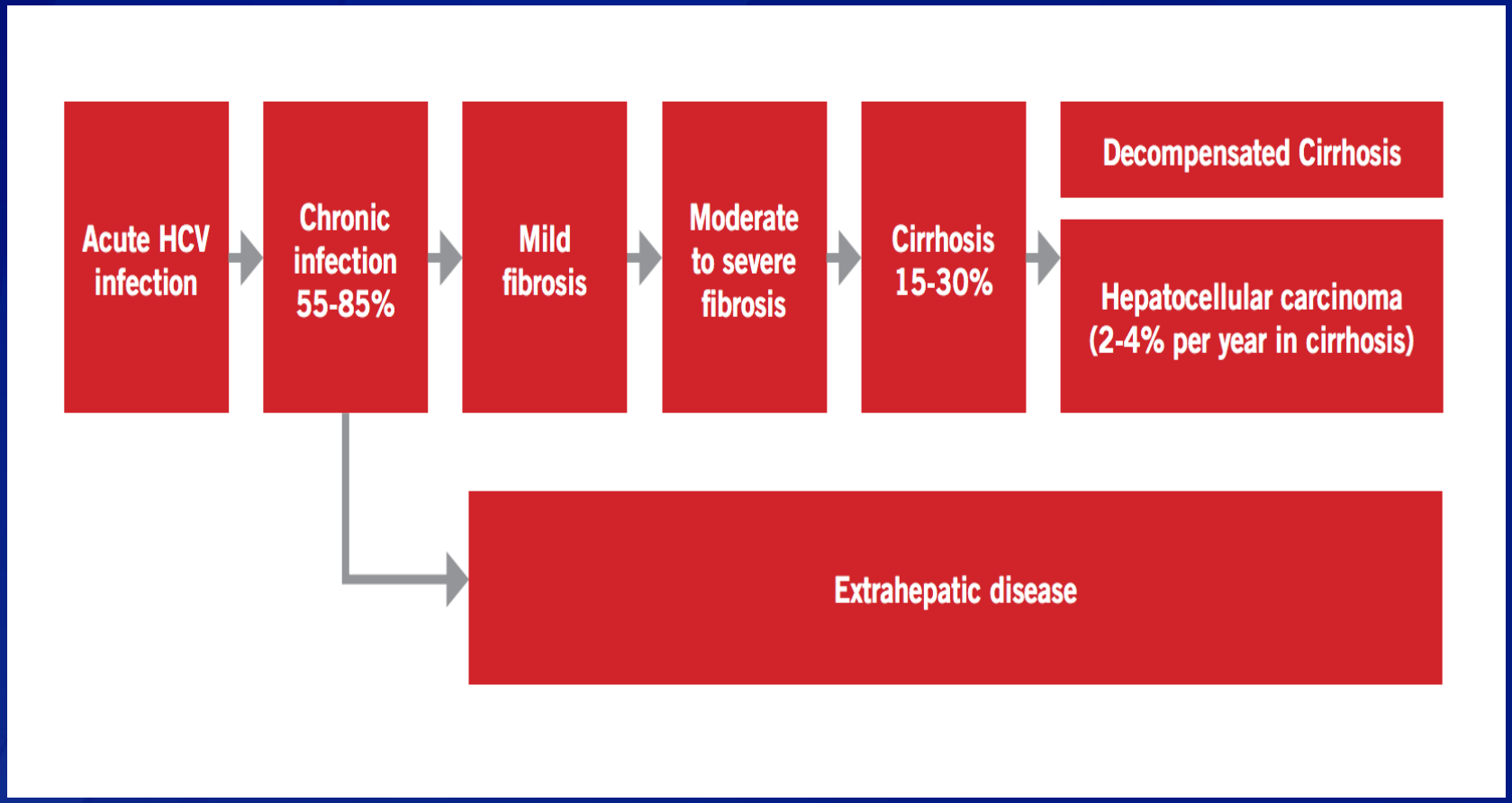
Denniston M, *Ann Int Med* 2014. Chak E, *Liver Int* 2011.

Natural History of HCV Infection



HIV, HBV, alcohol, and steatosis can accelerate disease progression

ESLD: End-stage liver disease. HCC: Hepatocellular cancer. HIV: Human immunodeficiency virus. HBV: Hepatitis B virus.

. Fattovich G, Gastroenterology 1997; NIH Consensus Statement. June 2002. http://www.who.int/hiv/pub/hepatitis/

Modes of HCV Transmission

- **Health care exposures- most common cause globally**
- **Injection drug use – highest risk population**
- **Other modes**
  - Sexual
    - Heterosexual -rare
    - HIV+ MSM have eight fold higher risk than HIV-MSM
  - Perinatal - ~4% transmission risk; ~12% with high maternal viral load
- Others reported
  - Non-injecting drug use (e.g., inhaled drugs)
  - Household exposures
  - Unregulated tattooing

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MSM: Men who have sex with men.

Scheinmann, Drug and Alcohol Dependence 2006. Weinbaum ,MMWR 2003. Gough, BMC Public Health 2010. Mast, J Infect Dis, 2005. Marincovich B, Sex Transm Infect 2003. Yaphe S, Sex Transm Inf 2012. Bottieau, Eurosurveillance 2010. Ackerman Z, J Viral Hepat 2000. Tohme RA, CID 2012 ; CDC/hepatitis.gov; CDC MMWR 2001

Healthcare-associated HCV Transmission

- Larger contributor to transmission before viral discovery
- Prevention measures have reduced not eliminated transmission risk
- Total 18 outbreaks reported to CDC 2008-2013
  - 223 outbreak-associated cases
  - >90,550 at-risk persons notified for screening
  - Settings
    - Outpatient (e.g., surgical centers), dialysis
    - Hospitals
    - Long term care
  - Modes of transmission
    - Syringe reuse
    - Other poor infection control
    - Drug diversion

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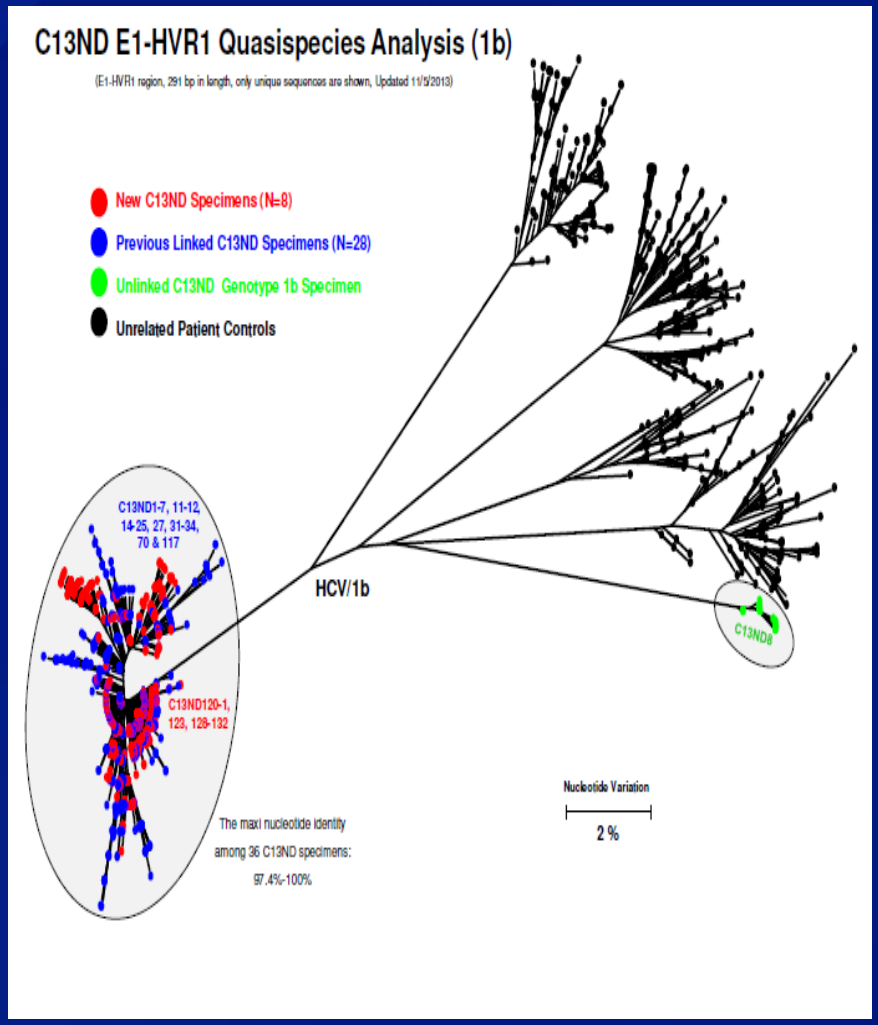
Outbreaks of HCV in Residential Care Settings

- Investigation of residential care facility- North Dakota
- 35 HCV cases identified; >25% prevalence
- Highly related HCV quasispecies
- Associated with podiatry exposures



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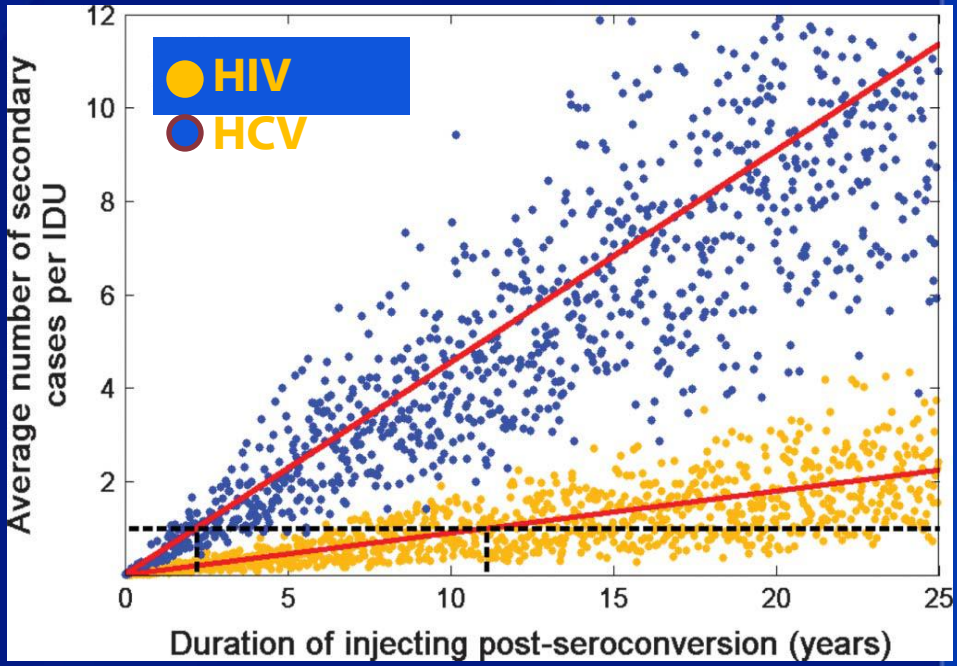
HCV Transmission Among Persons Who Inject Drugs

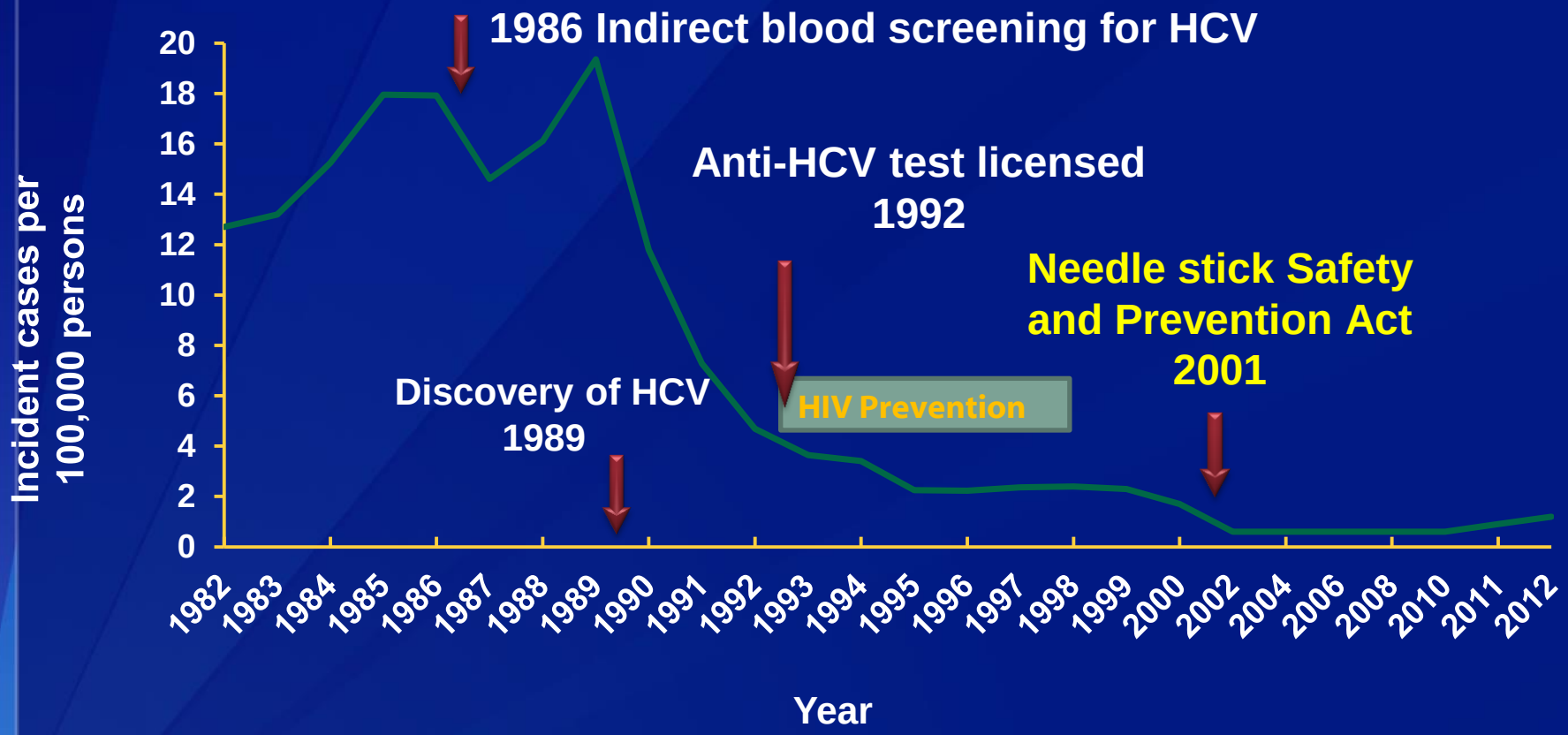
- Transmission risks
  - Injection duration
  - Frequency of injecting
  - Equipment sharing, not just sharing needles



- Incidence declined in response to harm reduction for HIV (e.g., syringe access programs)

Hagan, et al, Int J Drug Policy 2007; Hagan et al, Amer J Public Health 2001.; Lucidarme, et al, Epid and Infect 2004; Burt et al, J Urban Health 2007; Garfein R, J Urban health 2013; Keen L Addict Behav. 2014; Amon JJ, Clin Infect Dis 2008
Kwon et al., *JAIDS* 2009

Discovery of HCV and Impact on HCV Incidence in US

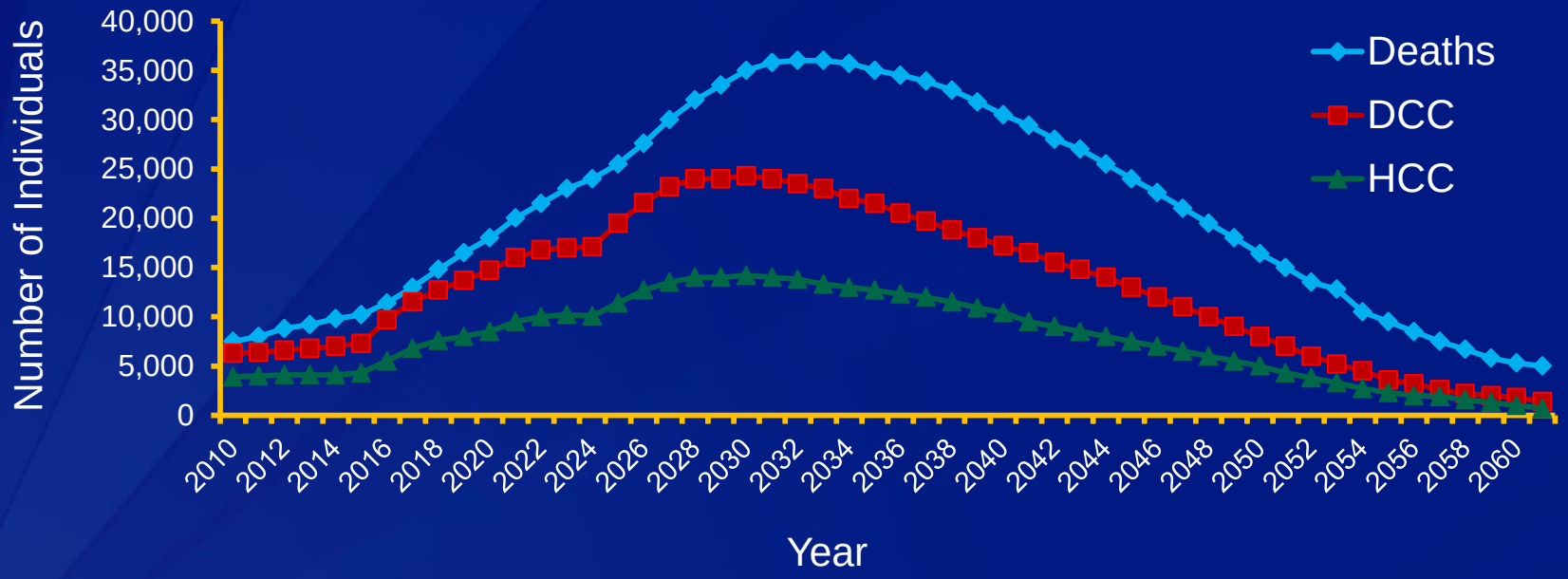


29,000 cases of incident HCV infection reported in 2013

Alter MJ JAMA 1990; Jagger J, J infect Dis Pub Health 2008;; Ward JW. *Clin Liver Dis,* 2013. CDC.gov/hepatitis;

The Growing Burden of Hepatitis C in the United States

- **Of 2.7 million HCV-infected persons in primary care**
  - —1.47 million will develop decompensated cirrhosis (DCC)
  - —350,000 will develop hepatocellular carcinoma (HCC)
  - —897,000 will die from HCV-related complications



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Rein D, *Dig Liver Dis* 2010.

Increases in Hepatitis C Mortality

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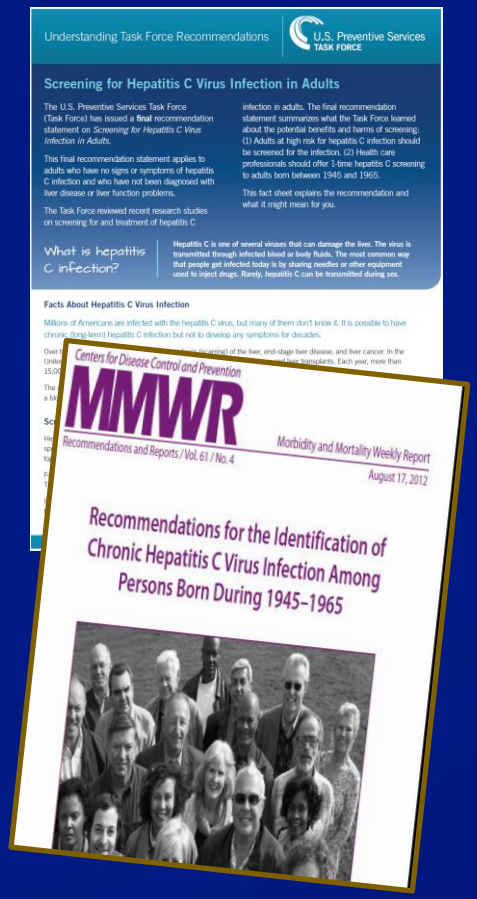
CDC and USPSTF Updated Recommendations for HCV Testing

- **One time screening test for persons born 1945-1965**
- **Major risk**
  - Past or present injection drug use
- **Other risks**
  - Received blood/organs prior to June 1992
  - Received blood products made prior to 1987
  - Ever on chronic hemodialysis
  - Infants born to HCV infected mothers
  - Intranasal drug use
  - Unregulated tattoo
  - History of incarceration
- **Medical**
  - Persistently elevated ALT
  - HIV (annual testing)



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MMWR Aug 2012. Moyer VA, *Ann Int Med* 2013.
http://www.hcvguidelines.org

Staging of HCV-Related Liver Fibrosis Using FIB-4 by Birth Cohort, 2010-2013

	Born<1945		Born 1945-1965		Born >1965		Total	
	Number	Percent	Number	Percent	Number	Percent		Percent
None	79	1	7,315	9	16,587	53	23,981	19
Moderate	1,543	19	32,996	38	8,949	29	43,488	35
Severe	2,982	37	22,448	26	2,172	7	27,602	22
Cirrhosis	2,865	36	17,875	21	1,315	4	22,055	18
Unknown/ missing	508	6	5,253	6	2,189	7	8,164	7
Total	7,977		85,887		31,212		125,290	

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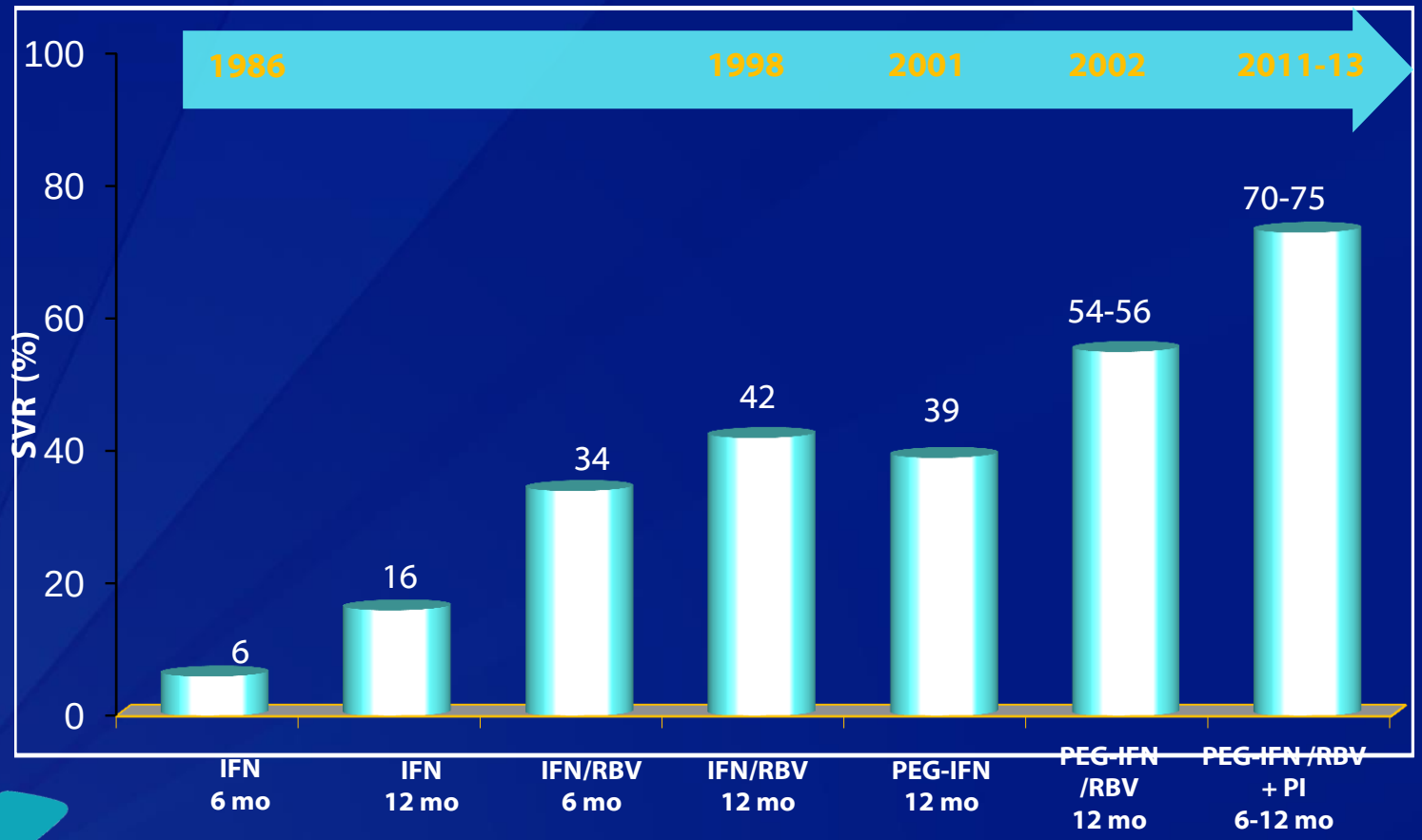
Monina K, CROI 2015

The Evolution of HCV Therapy from Interferon to Direct Antiviral Agents



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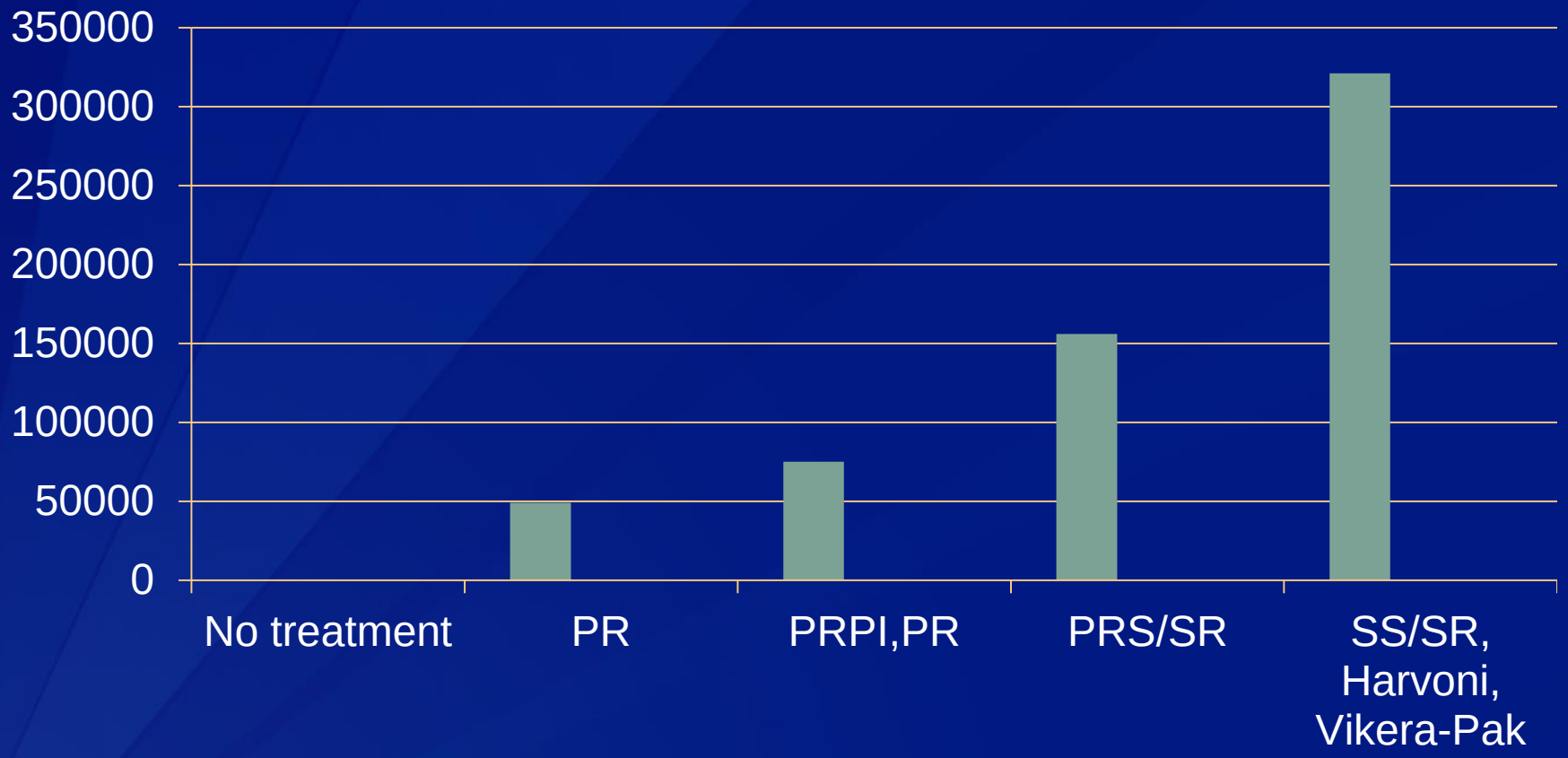
Strader DB, et al. Hepatology 2004;39:1147-71.

Potential to Avert 320,000 Deaths with Birth Cohort Testing Using Latest Treatments



PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI; PR = PR plus a protease inhibitor for genotype 1, PR for genotypes 2/3;
PRS/SR = pegylated interferon, ribaviron, and sofosbuvir for genotype 1, and sofosbuvir plus ribavirin for genotypes 2 and 3;
SS/SR = Sofosbuvir and Simeprevir for genotype 1, and sofosbuvir and ribavirin for genotypes 2 and 3.

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Testing of Persons Born 1945-1965 is Cost Effective (CE)

- Typical willingness-to-pay thresholds (<$50K-100K/QALY)
  - Treat all -31,828-35,100/QALY at market price (Vikera-Pak-$31,828,Harvoni $35,100
- Cost/QALY sensitive to stage of liver disease
  - F0- $173K; F2; $37K; F4- $13K; treat all $42 KI
- Drug costs are now lower than wholesale marker price
  - Payer/Pharma agreements- average ~46% decline
  - Medicaid- mandated 23% discount or to match best price
  - Lawsuits against health plans filed by patients denied treatment

*Quality adjusted life year.

Rein D. CID2015; Najafzadeh M *Ann Int Med.* 2015; Leidner Hepatology 2015; http://blogs.wsj.com/pharmalot/2015/02/12/; http://blogs.wsj.com/pharmalot/2015/05/26/

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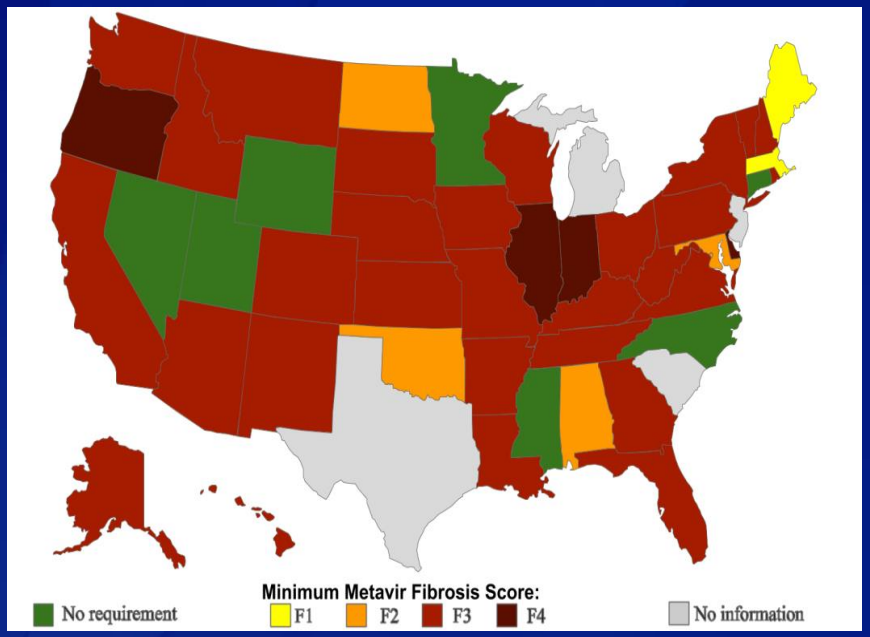
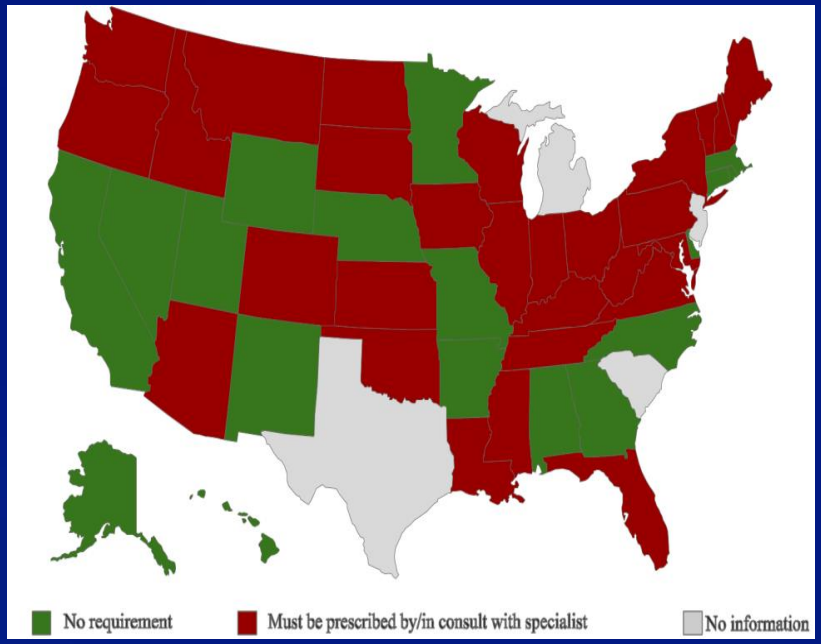
Medicaid Reimbursement Criteria- HCV Therapy

- Minimum fibrosis score
- Prescription by specialist





Some states have few specialists; some states require biopsies for fibrosis scoring

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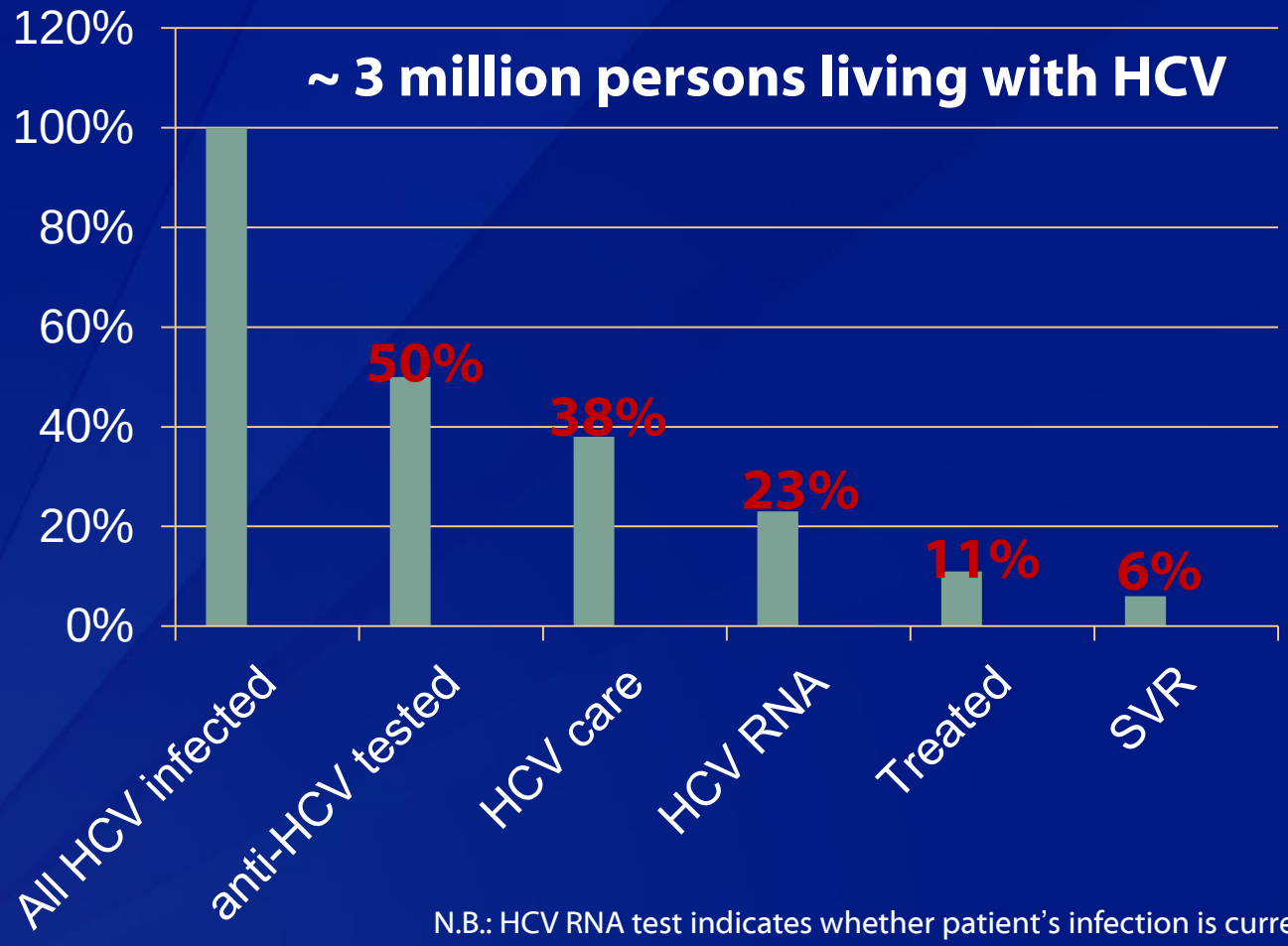
Canary L, Ann Int Med, in press

The Quality of HCV Management Must Improve for Patients to Benefit from HCV Therapy



N.B.: HCV RNA test indicates whether patient's infection is current or not.

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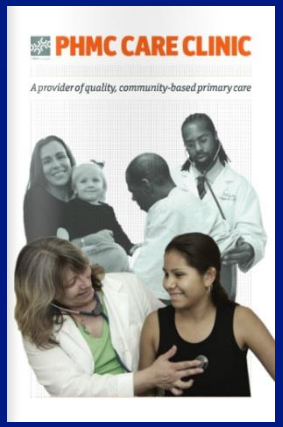
Holmberg S, et al, NEJM, 2013)

Philadelphia HCV Testing and Care Coordination

- **5 community health centers- Philadelphia**
- **Underserved, largely Black / Hispanic population**
  - ~75% homeless, 37% uninsured, 58% public insurance
- **Interventions**
  - Reflex HCV testing
  - Patient education
  - EMR prompts
  - Mid level provider conducting testing
  - Linkage to care coordinator
  - Uninsured: Referred to social worker



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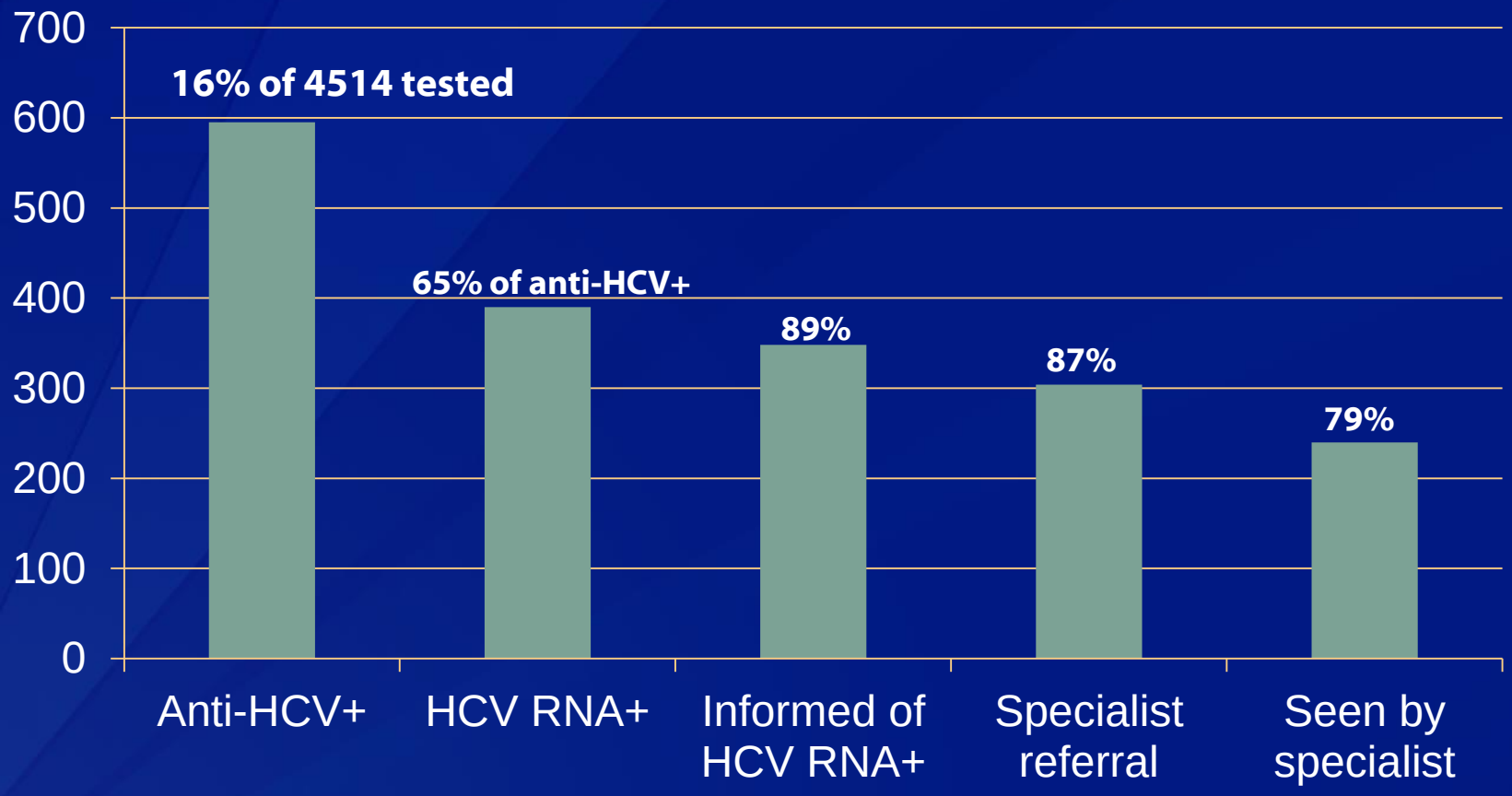
MMWR, May 2015

Philadelphia HCV Testing and Care Coordination



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MMWR, May 2015

Reports of Acute Hepatitis C Cases — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)

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CDC

Recent CDC, State, and Local Public Health Investigations of Young PWID

Location	Year	Predominant Race/Ethnicity	Predominant Setting	Virus
Northern Plains	2008	American Indian	Rural	HCV
Erie County, NY	2007	White	Suburban	HCV
Massachusetts	2011	White	Suburban	HCV
Wisconsin	2011	White	Rural	HCV
Indiana	2011	White	Rural	HCV
Virginia	2012	White	Rural	HBV +/- HCV
Courtland County, NY	2014	White	Rural	HCV

Common Denominator: Prescription opioid misuse followed by early initiation to injection drug use

Centers for Disease Control and Prevention. Notes from the field: hepatitis C virus infections among young adults—rural Wisconsin, 2010. MMWR Morb Mortal Wkly Rep 2012;61:358–358.

Centers for Disease Control and Prevention. Notes from the Field: risk factors for hepatitis C virus infections among young adults—Massachusetts, 2010. MMWR Morb Mortal Wkly Rep 2011;60:1457–58.

Centers for Disease C, Prevention. Use of enhanced surveillance for hepatitis C virus infection to detect a cluster among young injection-drug users--New York, November 2004–April 2007. MMWR Morb Mortal Wkly Rep 2008;57(19):517–21.

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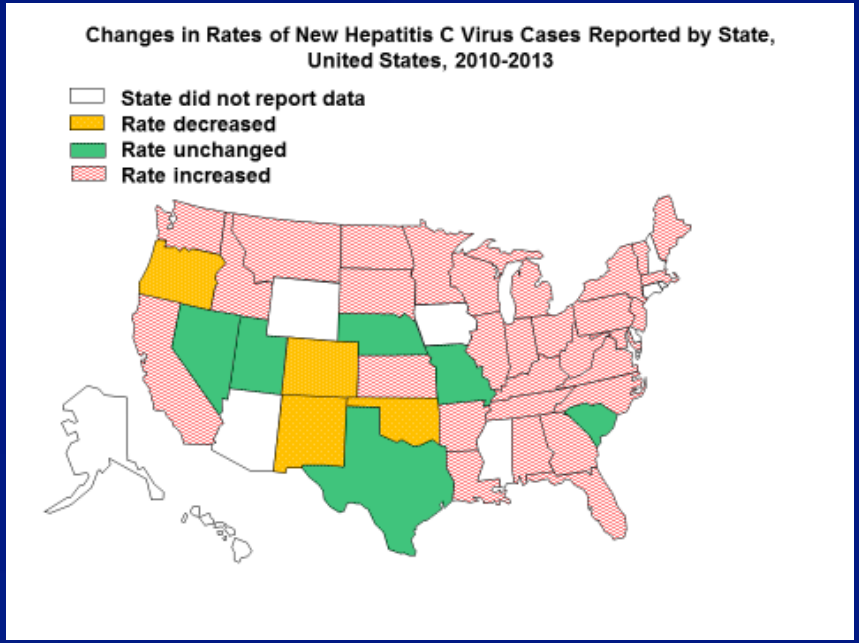
Surveillance of Acute HCV Infection - 2013

- Estimated 29,000 new HCV infections
- 150% increase since 2010
- 28 of 34 states reported increases

- 66% of cases reported from 12 states
  - (CA, FL, IN, KY, MA, MI, NJ, NY, NC, OH, PA, TN)
  - KY has highest rate

- Case Rates
  - 61% report IDU
  - Equal Male (0.8): Female (0.7)
  - Highest rate
    - by age 20-29 years, 2.01
    - By race American Indian (1.7) and whites (0.82)



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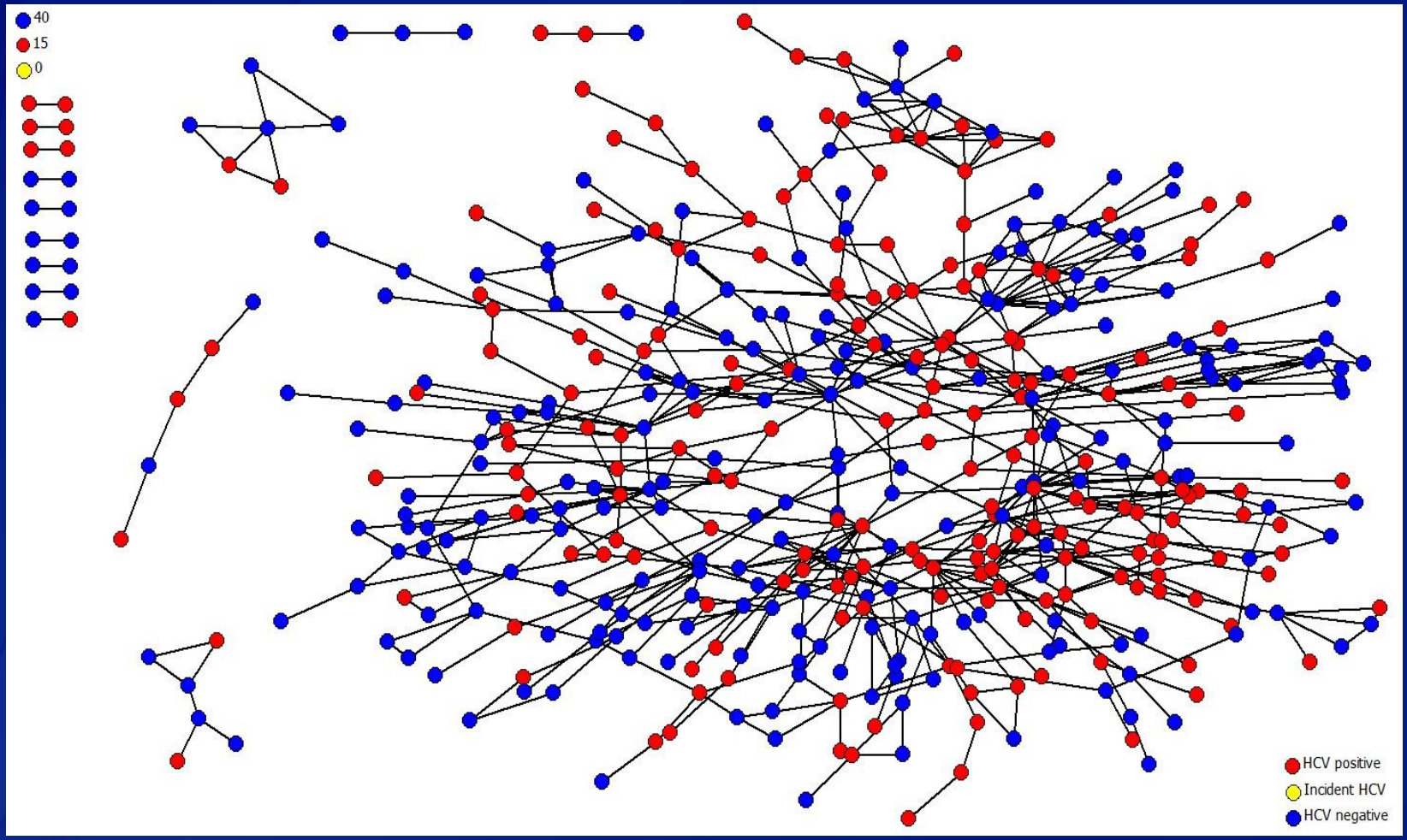
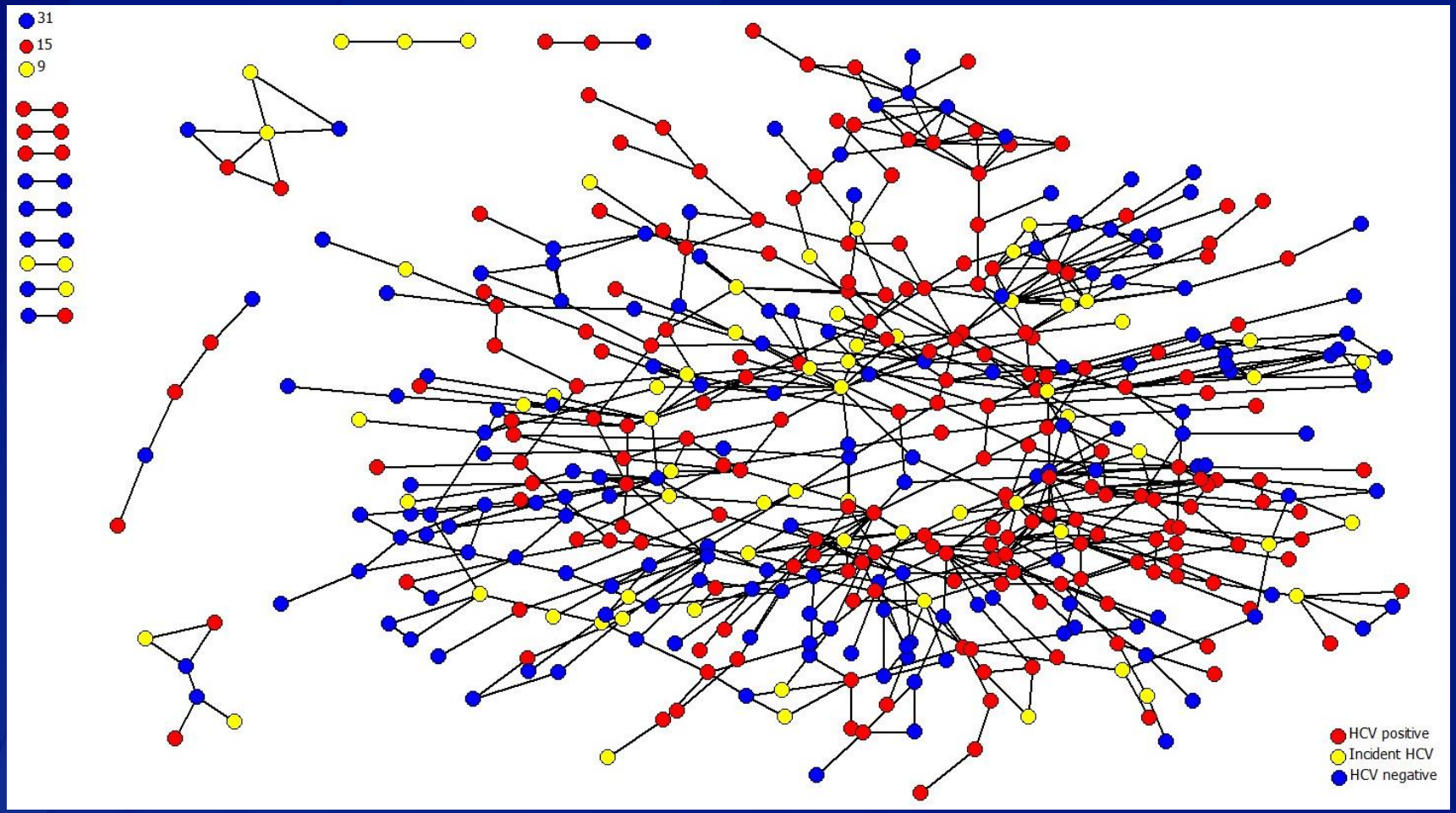
Tracking and Intervening to Prevent HCV
Social Network of IDU- rural Kentucky- baseline



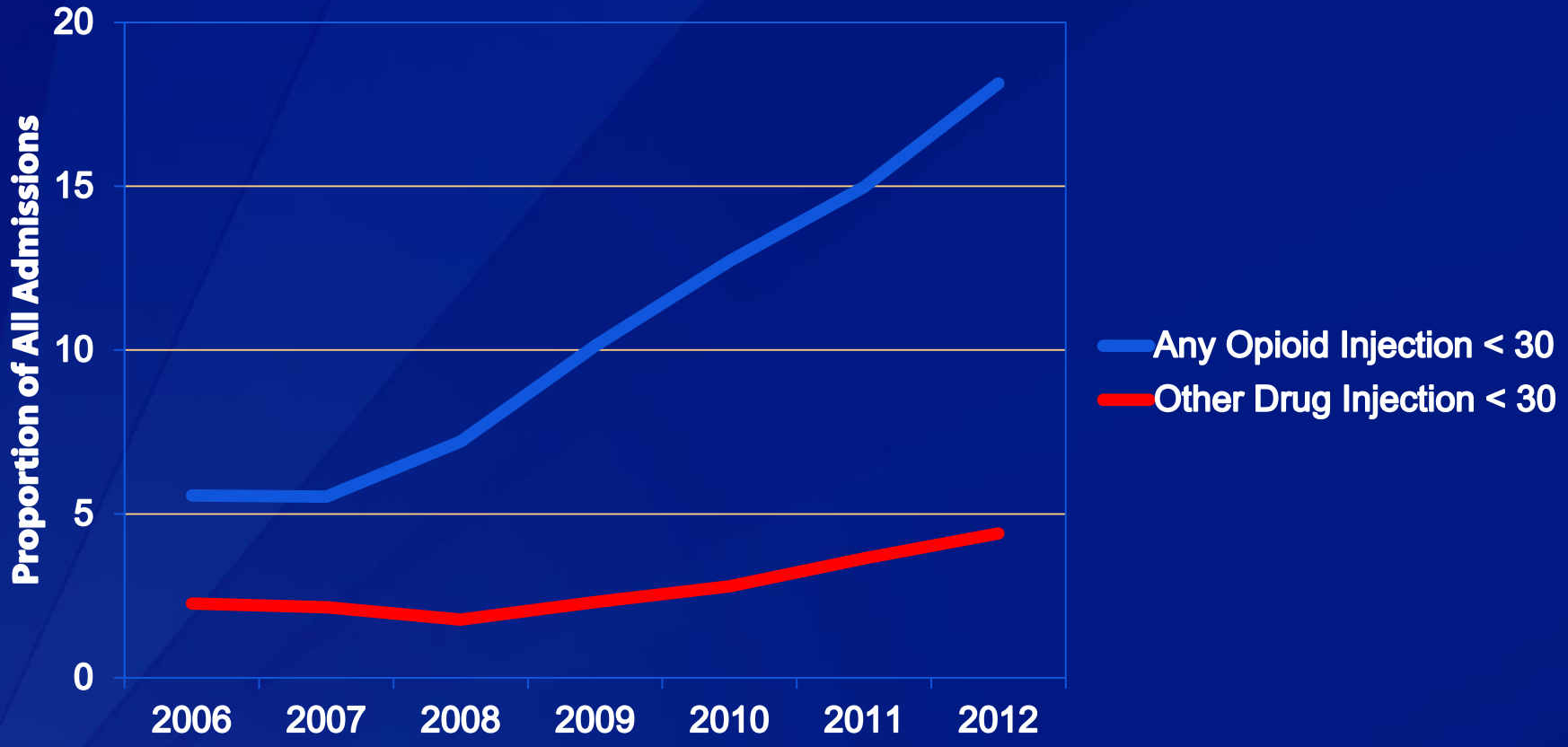
J Havans, NIDA R01-DA024598 and R01-DA033862

Understanding Transmission Among IDU
Social Network of IDU- rural Kentucky- 24-Month



J Havans, NIDA R01-DA024598 and R01-DA033862

Regional Drug Injection Trends Among Persons <30 years old in KY, TN, VA, WVA



SAMHSA, Treatment Episode Data Set—Admissions

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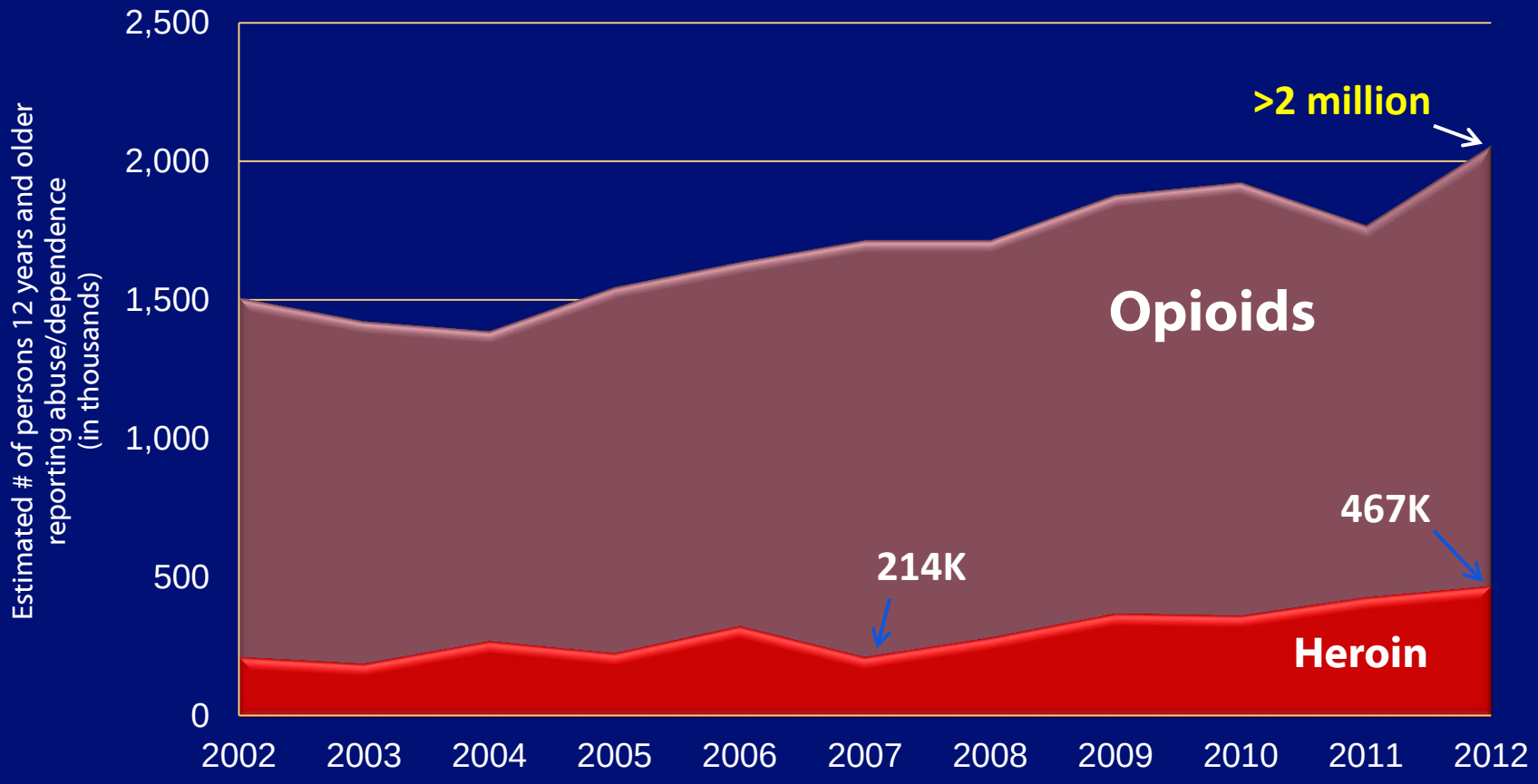
Heroin Use and Dependence is Increasing



SAMHSA NSDUH 2012

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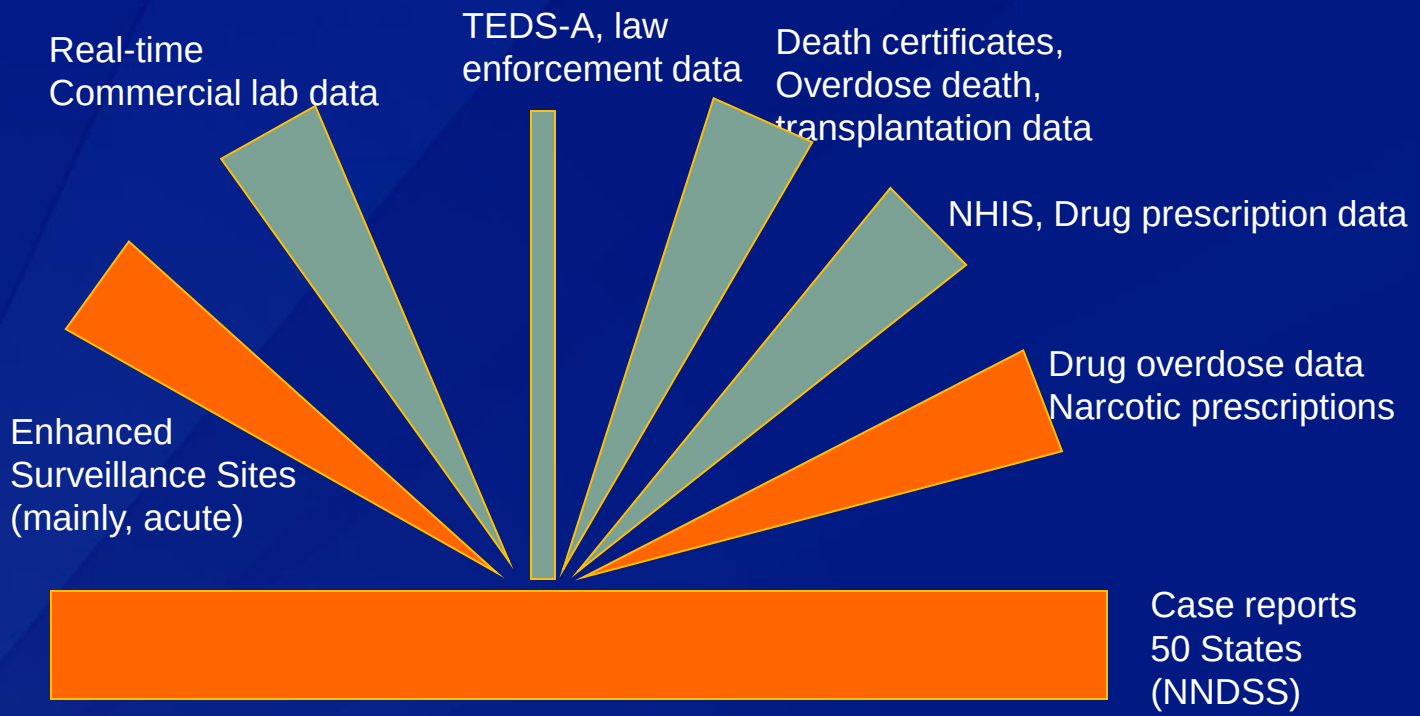
Analysis of Multiple Data Sources to Detect HCV Transmission and Related Risks



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Multi-Component Interventions Appear Most Effective in Preventing HCV Transmission

- In meta-analysis of single interventions, evidence only supports drug treatment

- A combination of *readily-available* and *low threshold* OAT (with methadone and/or buprenorphine) and SEPs have been shown to:
  - Reduce syringe sharing
  - Lower injecting risk
  - Reduce incidence of HIV and HCV
    - Up to 80% in UK
    - Three fold - New York

OAT: Opiod Agonist Treatment
SEP: Syringe Exchange Programs

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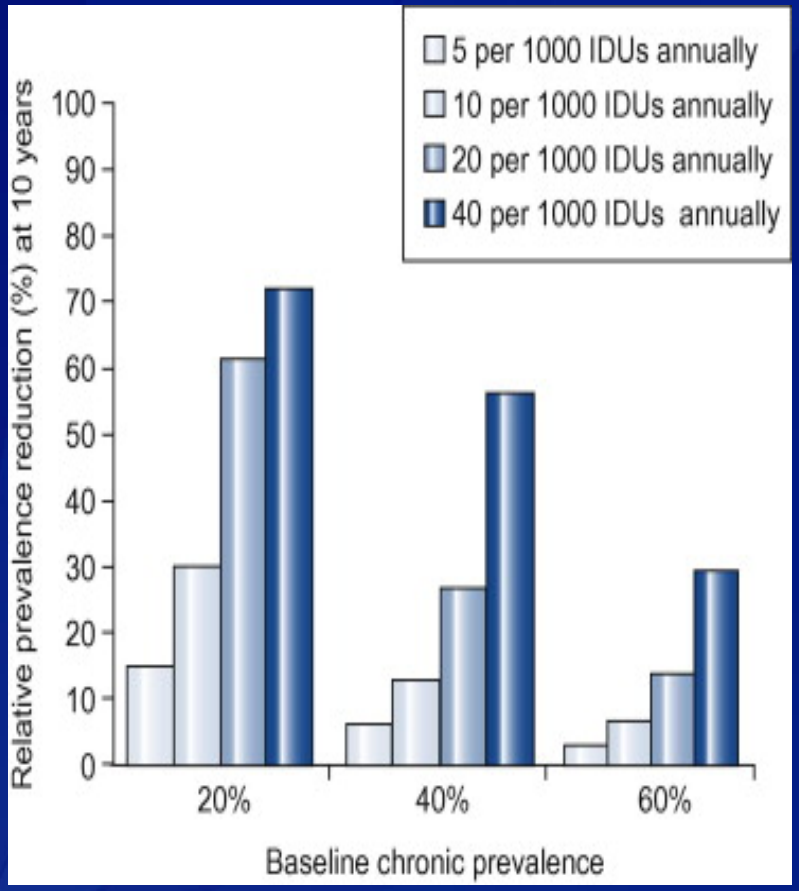
Palmateer N, Addiction. 2010; Degenhardt L, Lancet. 2010; Kwan JA, J Acquir Immune Defic Syndr. 2009; Turner KM Addiction. 2011; DesJarlais DC, The Lancet, MacArthur GJ, Int J Drug Policy 2014

Antiviral Therapy Might Be Used to Reduce HCV Prevalence Among Injecting Drug Users



- Annually treating 10 HCV infections per 1000 IDU and achieve SVR of 62.5%
- Projected to result in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% for prevalences of 20%, 40%, or 60%, respectively
- Can the HIV model of “Treatment as Prevention”be applied to HCV?

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Martin et al. Journal of Hepatology 2011 vol. 54 ¡ 1137–1144

HCV Screening & Testing at Venues Serving PWID

*Prevention and Public Health Fund**

January 2013—March 2014

Location	# of Tests	% anti-HCV+	% RNA Tested	% RNA +	% Referred to Care	% Attended First Appt.
Arizona	938	17.3	15.4	76.0	84.2	26.3
Chicago	672	22.2	40.9	80.3	51.0	0.0
Los Angeles	2175	8.7	29.6	89.3	100.0	82.0
Maine	795	28.1	51.1	60.5	98.6	52.2
New York City	2527	17.6	63.4	71.3	71.1	23.4
Oakland, CA	579	32.0	18.4	82.4	100.0	21.4
Seattle, WA	457	56.9	30.0	66.7	86.5	5.8
Virginia	761	36.8	75.4	78.2	99.4	27.3
Wisconsin	1127	16.1	107.1	73.3	100.0	100.0
Total	**10031**	**20.7%**	**50.9%**	**73.5%**	**87.9%**	**42.0%**

Venues Include**:** Syringe Exchange Programs; Drug Treatment Centers; Health Departments; Methadone Clinics; Corrections; Shelters

***CDC unpublished data**

HIV HCV Outbreak in Scott County, Indiana, 2014-2015

Status	# Patients	% among persons tested for both HIV and HCV
HIV-Positive/HCV-Positive	79	26%
HIV-Positive / HCV-Negative	3	1%
HIV-Negative / HCV-Positive	106	35%
HIV-Negative/HCV-Negative	111	37%
TOTAL SAMPLES	299	
	Anti-HCV-positive	%
High-Risk Patients (reported IDU)	185 / 299	62%
HIV-Coinfected	79 / 82	96%

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HCV antibody results

Activities to Improve Prevention of HCV Transmission in Scott County, IN

- Complete studies of social networks of HCV transmission
- Scale-up drug treatment, harm reduction
- Assess benefits of HCV cure and prevent (CAP)
  - Clinical capacity to treat target number of PWID
  - Ancillary prevention services
  - Drug availability
- Consider a CAP demonstration project

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Legal Intervention-Syringe Services Programs

- On March 24, 2015 the Kentucky General Assembly gave municipalities authority to institute a syringe exchange program

- Indiana passed a law in May allowing counties to seek state approval to run needle exchanges, if they are in the bottom two quartiles among Indiana Counties for average number of newly reported cases of hepatitis C before an exchange can be launched

https://louisvilleky.gov/government/health-wellness/needle-exchange-program; http://blogs.law.harvard.edu/billofhealth/2015/05/21/a-needle-in-a-haystack-finding-the-elusive-solution-to-indianas-hiv-outbreak/

Effective Prevention Strategies and Advent of Curative HCV Therapies Have Increased Considerations for HCV Elimination

Georgia as a Site to Model HCV Elimination

- - ~4 million persons
- High burden of HCV- 5-7%
- Relatively small in-migration
- Mixed infection risks- healthcare, IDU
- Capacity- modest, good record in HIV prevention
- Motivated government and population

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HCV Elimination in Georgia

- **Phase I: Immediate introduction of curative treatments (0 – 12 months)**
  - —Reduce morbidity and mortality by treating persons with severe HCV associated liver disease
  - —Build knowledge base for expanded access program
  - —Develop broader elimination plan (Phase II)

- **Phase II: Achieve HCV elimination (7-10 year time frame)**
  - —Define measurable/achievable goals
  - —Interventions to prevent new infections
  - —Expand access to treat all HCV infected persons

Proposals for HCV Elimination- United States

- **Increase priority -** widen public recognition of urgency of action
- **Increase screening -** follow USPSTF recommended screening
- **Improve testing algorithm -** simplify HCV screening and diagnosis
- **Enhance surveillance -** change policies to improve utility of data
- **Expand clinical workforce -** allow for primary care management
- **Increase treatment availability -** modify treatment regimens
- **Reduce payer restrictions –** increase number of therapeutics

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Phil Coffin, UCSF, CDC National HCV Summit – 6/2014)

HCV Elimination in Cherokee Nation

- Small population (314,000) in defined 14 county area
- 95% receive care in CN Health Service- hospital, 8 clinics
- High prevalence- anti-HCV 6.0% (2013); 5160 current HCV infections
- Nascent test, care, and cure programs
- Tribal leadership commitment to HCV elimination
- Coalition of public health, clinical care, and academic medicine

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Summary

- The burden of HCV mortality is large and growing
- HCV incidence is increasing in the US; IDU is major risk
- Effective interventions are available to prevent transmission and disease
  - Prevent mortality – Testing linkage to care and treatment
  - Prevent transmission – Infection control, harm reduction, drug treatment, cure and prevention strategies
  - HCV surveillance and monitoring data needed to guide interventions
- With capacity and commitment, elimination of Hepatitis C can become a feasible goal for the nation.

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Contributors

- Dan Church
- Jennifer Havans
- Scott Holmberg
- Saul Karpen
- Anil Suryprasad
- Jon Zibbell

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OPEN YOUR WORLD.
Most don't know they're infected
SIEMENS
ends a simple blood test for Hepatitis C, a silent killer.
Worker Doubts Oly
's Court Outbursts Are an Act
NEWS
to fans
ESPN
triners affiliate finishes 16-run comeback
SEPHORA